

# Binaphthol-derived Titanium $\mu$ -Oxo Complex: a New Type of Asymmetric Catalyst for Carbonyl-ene Reaction with Glyoxylate

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The binaphthol (binol)-derived chiral titanium  $\mu$ -oxo complex **O** is obtained accidentally upon toluene azeotropy from a solution of binol and  $(\text{Pr}^i\text{O})_2\text{TiCl}_2$  after filtration of  $m_s$  4 Å and shown to be an efficient asymmetric catalyst for the glyoxylate-ene reaction with  $\alpha$ -methylstyrene to give 98.7% enantiomeric excess and 88% yield even by the use of 0.2 mol% of the complex **O**.

Development of an asymmetric catalyst for carbon-carbon bond formation, in particular, is the most challenging and formidable endeavor in organic synthesis.<sup>1</sup> We have recently

developed an enantioselective catalysis of carbonyl-ene reaction with glyoxylate catalysed by the binaphthol-derived chiral titanium dihalide complexes **X**, which provide an efficient access to the asymmetric synthesis of  $\alpha$ -hydroxyesters of biological and synthetic importance.<sup>2</sup> We now report a binaphthol-derived chiral titanium  $\mu$ -oxo complex **O**, which is obtained accidentally and found to be an efficient asymmetric catalyst for the glyoxylate-ene reaction.

The chiral titanium dihalide catalysts **X** have been prepared *in situ* from optically pure binaphthol (binol) and diisopropoxytitanium dihalide  $[(\text{Pr}^i\text{O})_2\text{TiX}_2; \text{X} = \text{Br}$  or  $\text{Cl}]$  in the presence of molecular sieves ( $m_s$  4 Å).<sup>2</sup> We have thus examined the isolation of **X** through azeotropic removal of propan-2-ol (toluene, 110 °C) from a toluene solution of binol and  $(\text{Pr}^i\text{O})_2\text{TiCl}_2$  after filtration of  $m_s$  4 Å employed for the alkoxy-ligand exchange, but surprisingly obtained the binol-derived chiral titanium  $\mu$ -oxo complex **O**. Complex **O** is shown to be an efficient asymmetric catalyst for glyoxylate-ene reaction with  $\alpha$ -methylstyrene even by the use of 0.2 mol% of complex **O** to give 98.7% enantiomeric excess (e.e.) of the ene product in 88% chemical yield [eqn. (1)]. Methylene-cyclohexane also provides the glyoxylate-ene product with >99% e.e. in 68% isolated yield using 1 mol% of complex **O**. Surprisingly indeed, the IR spectra of **O** show clearly the strong absorption at 770 and 791  $\text{cm}^{-1}$  of  $\mu$ -oxotitanium bonds (Ti-O-Ti) rather than Ti=O bands.<sup>3</sup> Consequently, the elemental analyses of **O** indicates essentially no content of chlorine atom [found: 1.2%, calcd. for the dichloride complex (**X**;  $\text{X} = \text{Cl}$ ): 17.6%]. These results suggest that the thermolysis of titanium dichloride with propan-2-ol would result in the formation of a titanium  $\mu$ -oxo complex.<sup>4</sup>

The  $\mu$ -oxo, namely dimeric nature of our binol-derived complex **O** is further proven by the vapour pressure osmometric molecular mass ( $M_r$ ) measurement in dichloromethane at 30 °C (Table 1).<sup>5</sup> Interestingly, the  $M_r$  of homochiral complex  $(R)(R)\text{-O}$  (Fig. 1,† A) prepared from enantiomerically pure binol was concentration dependent, ranging from 682 [calcd.  $696.4$  for  $(\text{C}_{20}\text{H}_{12}\text{O}_2\text{TiO})_2$ ] in 1.5  $\text{g l}^{-1}$  solution to 786 in 12  $\text{g l}^{-1}$  solution. By contrast, the  $M_r$  of the heterochiral

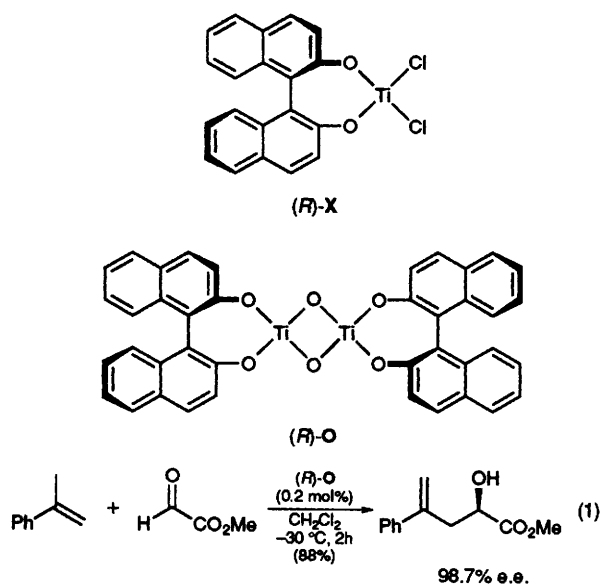


Table 1 Molecular mass of binol-derived titanium complexes **O**

<b>O</b>	Conc. $\text{g l}^{-1}$	Molecular mass
$(R)\text{-O}^a$	12.00	786
	6.00	752
	3.00	748
	1.50	682
$(\pm)\text{-O}^b$	11.64	811
	5.82	795
	2.91	793
	1.46	815

<sup>a</sup> Prepared from  $(R)$ -binol and  $(\text{Pr}^i\text{O})_2\text{TiCl}_2$ . <sup>b</sup> Prepared from  $(\pm)$ -binol and  $(\text{Pr}^i\text{O})_2\text{TiCl}_2$ .

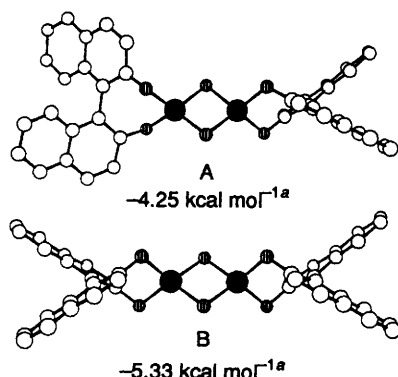


Fig. 1 3D Representation of  $(R)(R)\text{-O}$  **A** and  $(R)(S)\text{-O}$  **B**; 1 cal = 4.184 J. <sup>a</sup> Final steric energy.

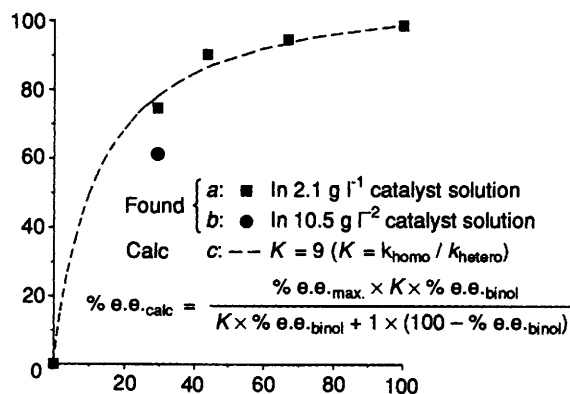


Fig. 2 Positive nonlinear effect in the glyoxylate-ene reaction with  $\alpha$ -methylstyrene

complex (*R*)(*S*)-**O** prepared from racemic binol was not concentration dependent, indicating the stability of the *meso* complex **B**. The concentration dependence of the  $M_r$  of homochiral (*R*)(*R*)-**O** implies that the homochiral complex is relatively unstable as shown by the higher steric energy calculated for **A** and hence dissociates to the monomeric form to some extent in dilute solutions. Thus, we have found a positive nonlinear effect<sup>6</sup> (asymmetric amplification) between e.e. values of binol employed and the glyoxylate-ene product, particularly in dilute solutions [Fig. 2(a)].<sup>7</sup> Furthermore, the observed relationship of e.e.s of the ene products to those of binol fits well with the nonlinear curve *c*, calculated on the basis of a 9 times rate (catalytic activity) difference ( $K = k_{\text{homo}}/k_{\text{hetero}} = 9$ ) between the homo- and hetero-chiral  $\mu$ -oxo complexes **O**.

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### Footnote

† The 3D structures of **A** and **B** were geometrically optimized with the Molecular Mechanics version 2 run on a Tectronix CaChe molecular modelling workstation.

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